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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/055,838	10/29/2001	Yingjian Wang		7868

7590 04/21/2006

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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,838	WANG, YINGJIAN	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-24 and 30-35* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 25-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-24 and 30-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-19 and 25-29 are withdrawn.

Claims 20-24 and newly added claims 30-35 are pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 20 and 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Meade, 6,248,229.

More specifically, as to claim 20, Meade teach a method of detecting proteins comprising the steps of immobilizing a plurality of different ligands (col. 17, lines 34-35) on a solid support (col. 17, line 35, and line 26) at separate known site on a solid support (col. 17, line 28, disclosing an array form); incubating said ligands on said solid support with a sample having said proteins, wherein said ligands bind said proteins (col. 18, line 66 – col. 19, line 4); covalently cross-linking said ligands and said proteins with a cross-linker (col. 19, lines 27-34); and detecting said proteins (col. 21, lines 4-6).

As to claim 22, said ligands are antibodies (col.7, lines 22-24.)

As to claim 23 and 24, the number of said ligands ranges from 1 to 1,000,000 or from 100 to 10,000, (col. 17, lines 37-41).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meade, 6,248,229, in view of Gorman et al., 6,562,578.

Meade disclose the invention substantially as claimed (see above with respect to claim 20). Meade teaches that the binding ligand may be a protein, antibody, or a partner of a receptor-ligand pair (col. 7, lines 19-24.) However, Mead does not teach that the ligands are recombinant proteins.

Gorman et al. however teach that assays using recombinant antigen are useful in a variety of drug screening techniques. Gorman et al. teach that the advantages of using a recombinant protein in screening for specific ligands include: (a) improved renewable source of the antigen from a specific source; (b) potentially greater number of antigen molecules per cell giving better signal to noise ratio in assay; and (c) species variant specificity theoretically giving greater biological and disease specificity (col. 46, lines 11-19). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize recombinant antigens as taught by Gorman et al. in the

Meade invention because Gorman et al. teach that using recombinant protein provides the advantages of (a) improved renewable source of the antigen from a specific sourcek, (b) potentially greater number of antigen molecules per cell giving better signal to noise ratio in assay, and (c) species variant specificity theoretically giving greater biological and disease specificity.

3. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meade, 6,248,229, in view of Wallace et al., 4,424,208, and further in view of Weissman et al., 5,213,977.

Meade disclose the invention substantially as claimed (see above with respect to claim 20). Moreover, Meade teaches that bifunctional agents such as maleimidobenzoic acid may be used to cross-link peptides (col. 19, lines 31-34). However, Meade does not list glutaraldehyde as an example of a cross-linker.

Wallace et al. however teach that glutaraldehyde is commonly used to cross-link proteins for medical use (col. 3, lines 2-5). Moreover, Weissman et al. teach that joining proteins together is well known in the art and a variety of linking groups are available such as glutaraldehyde and formaldehyde and maleimidobenzoic acid (col. 4, lines 64-67.) Thus, Weissman et al. teach that glutaraldehyde is a functional equivalent to maleimidobenzoic acid in cross-linking proteins.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize glutaraldehyde as the crosslinker in the Meade invention because Wallace et al. teach that glutaraldehyde is commonly known to cross-link

proteins and Weissman et al. further teach that glutaraldehyde is a crosslinker that is a functional equivalent to maleimidobenzoic acid, which is listed by Meade as an example of a crosslinker. One of ordinary skill in the art would have reasonable expectation of success in utilizing glutaraldehyde to cross-link the antigen-antibody pair in the Meade invention given the teachings of Wallace et al. and Weissman et al. that glutaraldehyde is well known and commonly used as a cross-linker to crosslink proteins.

4. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meade, 6,248,229, in view of Kung et al, 5,436,319.

Meade discloses the invention substantially as claimed (see above with respect to claim 20). Meade teaches that binding ligands may be proteins, antibodies, or a partner of a receptor-ligand pair (col. 7, lines 19-24.) However, Mead does not teach that the sample is cell lysate prepared from cell lines or tissues.

Kung et al. however teach using immobilized antibodies to detect T cell antigen receptor in lysates from a variety of T cell lines (col. 22, lines 33-34). Kung et al. teach that detection of T cell antigen receptors may be used as a marker for the diagnosis and monitoring of certain disorders and diseases such as T cell malignancies and autoimmune diseases (col. 12, lines 47-56). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize antibodies in the Meade invention that specifically detect T cell antigen receptor in lysates from T cell lines as taught by Kung et al. because Kung et al. teach that such detection may be used for the diagnosis and monitoring of certain disorders and diseases such as T cell

malignancies and autoimmune diseases. One of ordinary skill in the art would recognize the desirability of diagnosing or monitoring T cell malignancies and autoimmune diseases for medical purposes.

5. Claims 20, 21, 31, 32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cook, 6,172,208, in view of Sluka et al., 5,851,840, and Huan et al., 6,696,246, and further in view of Meade, 6,248,229.

Cook discloses the invention substantially as claimed. More specifically, as to claims 20 and 31 and 32, Cook discloses a method of detecting proteins comprising the steps of incubating ligands (i.e., oligonucleotide conjugates, col. 13, line 57) with a sample having said proteins (i.e., proteins on col. 13, line 58) to allow the binding between said ligands and said proteins (col. 13, line 58), and detecting said proteins (col. 14, lines 7-9).

However, Cook does not teach immobilizing the oligonucleotides. That is, Cook does not explicitly disclose that the above embodiment utilizing an oligonucleotide *to detect a protein* includes immobilizing the oligonucleotide on a solid support. Cook does teach however an embodiment wherein the oligonucleotide is immobilized on a solid support for *detection of nucleic acid sequences* (col. 13, lines 15-21.) Cook teaches a series of washing steps in this embodiment (col. 13, lines 22-28). It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize the oligonucleotide in the embodiment wherein protein is detected as taught by Cook because one of ordinary skill in the art would recognize that

immobilization facilitates washing steps as disclosed by Cook, as would necessary to remove unwanted material during the assay. (Also, Sluka et al. provide a further motivation to immobilize oligonucleotides as discussed immediately below.)

Also, Cook does not teach immobilizing different oligonucleotides at separate known sites. Sluka et al. teach these limitations. Sluka et al. teach that different probes can be bound to individual spots on a solid support such that an analytical element is obtained which has different zones in a minimum space which are able to bind many different analytes to analyze a sample for different analytes (col. 11, lines 3-8 and col. 12, lines 36-40).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize different oligonucleotides in the Cook invention as taught by Sluka et al. in an array pattern (i.e., separate known sites) because Sluka et al. teach that such that an analytical element has different zones in a minimum space which can be used to analyze a sample for different analytes. One of ordinary skill in the art would recognize the desirability of requiring minimum space on an analytical device and the convenience of being able to analyze a sample for different analytes on a single device.

Also, Cook does not teach covalently cross-linking said ligands and said proteins (i.e., target analytes). Huan et al. teach immobilizing a plurality of oligonucleotides in an arrayed pattern (col. 11, lines 6-10 and lines 57-58) and using crosslinkers to covalently bind the probe to the target once binding has occurred facilitates washing steps (col. 11, lines 22-29) to improve sensitivity and reproducibility of the assay (col. 9, lines 60-67.)

Huan et al. give examples of crosslinking moieties (col. 11, lines 42-51.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide cross-linkers in the invention disclosed by Cook in view of Sluka et al. as taught by Huan et al. because Huan et al. teach that using crosslinkers to bind the probe to the target facilitates washing and improves sensitivity and reproducibility of the assay.

While Huan et al. do not specifically teach that cross-linkers can cross-link oligonucleotide probes and *protein* analytes, this limitation is taught by Meade. Meade teaches nucleic acid-binding protein (col. 7, lines 16-17) and that "chemical cross-linking after binding may be done, as will be appreciated by those in the art" (col. 19, lines 31-32). Meade gives examples of bifunctional agents that may be used as cross linkers (col. 19, lines 33-34). It would have been obvious to one of ordinary skills in the art at the time the invention was made to cross-link oligonucleotide probe and protein analytes in the invention disclosed by Cook in view of Huan et al. because Meade teach oligonucleotide-protein binding and chemical cross-linking after binding between a probe and an analyte. Given the examples of cross-linkers disclosed by both Huan et al. and Meade, one of ordinary skill in the art would have reasonable expectation of success in using cross-linkers to cross-link oligonucleotide probes to protein analytes.

As to claim 21, the references also do not disclose that one side of said support is specifically at least 1 millimeter long. However, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. In this case, the general conditions of the claim are disclosed by the prior art (Cook, Sluka et

al., Huan et al., and Meade) as discussed above, and the range of length of the support is an optimum or workable range and thus discovering this range involves only routine skill in the art.

As to claim 34, while Cook does not specifically disclose in the embodiment wherein the oligonucleotides are used to detect *proteins* that the oligonucleotides are immobilized on a nitrocellulose membrane, Cook however does teach immobilization of oligonucleotides on an inert solid support such as a nitrocellulose membrane in another embodiment wherein oligonucleotides are used to detect DNA hybridization (see col. 13, lines 19-21). It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide nitrocellulose as a solid support in the embodiment disclosed by Cook wherein the oligonucleotides are used to detect proteins because Cook teaches that nitrocellulose may be used to immobilize oligonucleotides and that nitrocellulose is inert. One of ordinary skill in the art would recognize that an inert material would be desirable as a solid support for an assay for more accurate results, as would be desirable in the invention as taught by Cook in view of Sluka et al., Huan et al. and Meade. (Moreover, Huan et al. also teach that immobilization may be done on nitrocellulose paper, see column 4, lines 33-34.)

Response to Arguments

Applicant's arguments with respect to amended claims 20-24 and newly added claims 30-35 have been considered but are moot in view of the new ground(s) of rejection. (Applicant states that the prior art in the previous Office action do not disclose

cross-linking between ligands and the proteins, as is recited in the amendments and newly added claims. Applicants argument is persuasive as to the previous prior art recited in the last Office action but are moot in view of the new grounds of rejection.)

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on M-Sat 11-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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